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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/749,873	12/29/2000	Toshihiko Ohtomo	053466/0294	6722

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EXAMINER	
HELMS, LARRY RONALD	
ART UNIT	**PAPER NUMBER**
1642	18

DATE MAILED: 11/07/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/749,873	Applicant(s) OHTOMO ET AL.	
	Examiner Larry R. Helms	Art Unit 1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 September 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 40-59* is/are pending in the application.

4a) Of the above claim(s) *1,44-47 and 53-57* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *40-43,48-52,58 and 59* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. *08/646,265* .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Claims 40 and 48 have been amended in the amendment filed 9/2/03.

Claims 58-59 have been added in the amendment filed 4/11/03

2. Claims 1, 44-47, 53-57 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention. Election was made and treated without traverse in Paper No. 9.

3. Claims 40-43, 48-52, and 58-59 are under examination.

4. The text of those sections of title 35, USC Code not included on the Office Action can be found in a prior Office Action.

5. The following Office Action contains NEW GROUNDS of rejections.

Rejections Withdrawn

6. The rejection of claims 40-43, 48-52 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention with respect to paragraph a in the previous Office action is withdrawn in view of the amendments to the claims.

Response to Arguments

7. The rejection of claims 40-43, 48-52 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention with respect to the term "derived" is maintained.

The response filed 4/11/03 has been carefully considered but is deemed not to be persuasive. The response states that the term derived is recognized in the antibody field and there are 1,270 patents with the term in claims (see page 4 of response). In response to this argument, the prosecution history of other patents is immaterial to the prosecution of the instant application. The term is not defined and can encompass deletions, substitutions, etc. In addition the claims do not require any binding to any particular antigen and as such the CDRs can be any sequence and as such the term derived encompasses altering any sequence.

8. The rejection of claims 40-42, 48-50, 58-59 under 35 U.S.C. 102(b) as being anticipated by Adair et al (WO 91/09967, published 7/91, IDS #2 ½) is maintained.

The response filed 4/11/03 has been carefully considered but is deemed not to be persuasive. The response states the Adair reference does not identify those residues important for antibodies with specificity for medulloblastoma cells and the invention teaches the exact residues that are necessary in the humanization of an antibody with specificity for medulloblastoma cells. The response further states that the Adair reference was published in 1991 and research presented in 1993 (Moriuchi, S. et al) concluded that research remained to be conducted regarding the three CDRs of the ONS-M21 and in 1993 the antigen recognition sites to make a humanized antibody specific for medulloblastoma cells was unknown and the Adair reference is non-enabling (see page 5 of response). In response to this argument, the claims do not require the antibody to bind medulloblastoma cells and as such any arguments directed to such are not on point. Therefore, Adair does not have to teach anything about

medulloblastoma or the ONS-M21, which is unclear what it has to do with the argument in addition to the Moriuchi et al reference which is incomplete. Adair et al teaches the method of humanization with substitution of the recited positions and as such reads on the claim and is enabled.

9. The rejection of claims 40, 43, 48, 51, 58 under 35 U.S.C. 102(e) as being anticipated by Seemann et al (U.S. Patent 5,645,817, Con to 8/93) is maintained.

The response filed 4/11/03 has been carefully considured but is deemed not to be persuasive. The response states Seemann et al does not teach that proline at position 46 on the L chain would increase the ability of the reshaped antibody to bind to medulloblastoma cells (see page 5 of response). In response to this argument, the claims recite nothing with regard to medulloblastoma cells. Thus the art of Seemann et al reads on the claims.

10. The rejection of claims 40-43, 48-52, 58-59 under 35 U.S.C. 103(a) as being unpatentable over Adair et al (WO 91/09967, published 7/91, IDS 2 ½) as applied to claims 40-42, 48-50 above, and further in view of Seemann et al (U.S. Patent 5,645,817, CON to 8/93) and Huston et al (WO 88/09344, published 12/88) is maintained.

The response filed 4/11/03 has been carefully considured but is deemed not to be persuasive. The response states that Adair teach a multitude of optional residues and Seemann does not teach that a proline mouse residue should be incorporated into

an antibody to target medulloblastoma cells and further it was not obvious the linker claimed in claim 48 would create an antibody specific for medulloblastoma cells (see page 6 of response). In response to this argument, again the claims recite nothing about the antibody being specific for medulloblastoma cells. In addition, Huston's linker would be generic and be used for any single-chain antibody and in fact claims the linker in a generic method to produce any single-chain antibody (see claim 39). Therefore, the art reads on the claims.

Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

11. The rejection of claims 40-43, 48-52, 58-59 under 35 U.S.C. 103(a) as being unpatentable over Moriuchi et al (British J. Cancer 68:831-837, 11/12/93, Ids # 2 ½) as evidenced from the specification and further in view of Adair et al (WO 91/09967, published 7/91, IDS 2 ½) and Huston et al (WO 88/09344, published 12/88) is maintained.

The response filed 4/11/03 has been carefully considered but is deemed not to be persuasive. The response states Moriuchi et al teaches the general positions that ONS-M21 would be helpful to produce a humanized antibody but does not identify the sequences of the three CDRs and Adair does not identify which mouse residues provide sufficient binding activity for an antibody with specificity for medulloblastoma cells and it would not be obvious to combine Adair with Moriuchi to obtain an antibody that binds medulloblastoma cells or combine this with Huston (see pages 6-7 of response). In

response to this argument, the claims do not recite the specific antibody or medulloblastoma cells. Although the claims do not recite the specific antibody ONS-M21, it would have been obvious in view of Adair to obtain the CDR sequences as well as the entire light and heavy chain sequences of the antibody (see page 13 of Adair) of Moriuchi and humanize it with the method of Adair and use the linker as taught by Huston to produce an antibody for human therapy.

The following is a NEW GROUND of rejection

Claim Rejections - 35 USC § 112

12. Claims 40-43, 48-52, 58-59 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 40-43, 48-52, 58-59 are indefinite for reciting "a mouse antigen binding site" in claim 40, 48, 58 because the exact meaning of the phrase is not clear. Claim 40 recites in part (c)and claim 48 part (a) and claim 58 part (c) "substituting 0-5 amino acid reside(s) on an H chain numbered according to Kabat with a mouse antigen binding site". It is unclear if the phrase means substituting any residues with an entire antigen binding site such as the CDRs or just substituting mouse residues for human frameworks or substituting mouse CDRS for human residues or some other meaning?. Likewise it is unclear in claim 48 part (a) and claim 59 part (a) what is meant by "substituting an amino acid residue at position 46 of an L chain V region numbered

according to Kabat, as a mouse antigen binding site" because it is not clear if position 46 is substituted with the CDRs of the mouse or position 46 is a mouse residue.

Conclusion

13. No claim is allowed.

14. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Larry R. Helms, Ph.D, whose telephone number is (703) 306-5879. The examiner can normally be reached on Monday through Friday from 7:00 am to 4:30 pm, with alternate Fridays off. If attempts to reach the examiner by

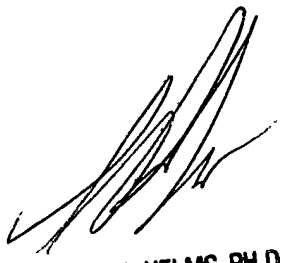
telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, can be reached on (703) 308-3995. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

16. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 308-4242.

Respectfully,

Larry R. Helms Ph.D.

703-306-5879



LARRY R. HELMS, PH.D
PRIMARY EXAMINER